

## AMENDMENT

Subject matter to be added is in bold and underlined.

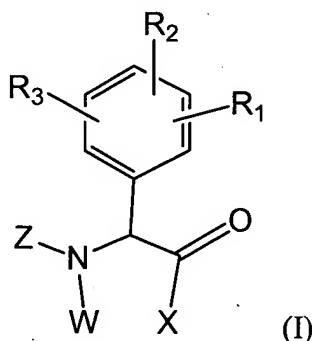
Subject matter to be deleted is in bold and strikethrough.

### In the Claims:

Please enter rewritten claims 19-21 as follows. Please cancel Claims 3-4, 22-36, and 51 without prejudice or disclaimer.

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Previously presented) A compound according to formula (I),



or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein:

X is  $-\text{NR}_6\text{S}(\text{O})_p\text{R}_{16}$ ;

W is hydrogen or  $-(\text{CR}_7\text{R}_8)_q-\text{W}_1$ ;

W<sub>1</sub> is hydrogen or may be taken together with R<sub>6</sub> to define a bond so that X and W are joined together to form a five to seven membered heterocyclic ring;

Z is isoquinolyl optionally substituted with 1-3 substituents selected from R<sub>9</sub> and/or R<sub>10</sub>;

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are attached to any available carbon atom of the phenyl ring and are independently selected from hydrogen, halogen, cyano, nitro, C<sub>1-10</sub>alkyl,

C<sub>2-10</sub>alkenyl, substituted C<sub>1-10</sub>alkyl, substituted C<sub>2-10</sub>alkenyl, -C(=O)NR<sub>12</sub>R<sub>13</sub>, -OR<sub>12</sub>, -CO<sub>2</sub>R<sub>12</sub>, -C(=O)R<sub>12</sub>, -SR<sub>12</sub>, -S(O)<sub>t</sub>R<sub>15</sub>, -NR<sub>12</sub>R<sub>13</sub>, -NR<sub>12</sub>SO<sub>2</sub>R<sub>15</sub>, -NR<sub>14</sub>SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, -NR<sub>12</sub>CO<sub>2</sub>R<sub>13</sub>, -NR<sub>12</sub>C(=O)R<sub>13</sub>, -NR<sub>14</sub>C(=O)NR<sub>12</sub>R<sub>13</sub>, -SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, aryl, heteroaryl, cycloalkyl, and heterocyclo;

R<sub>6</sub> is hydrogen, C<sub>1-4</sub>alkyl, NH<sub>2</sub>, C<sub>1-4</sub>alkylamino, hydroxy, or C<sub>1-4</sub>alkoxy, or together with W<sub>1</sub> is a bond so that X and W join together to form a five to seven membered heterocyclic ring;

R<sub>7</sub> and R<sub>8</sub> are independently selected from hydrogen, -OR<sub>18</sub>, -NR<sub>18</sub>R<sub>19</sub>, -NR<sub>18</sub>SO<sub>2</sub>R<sub>20</sub>, alkyl, alkenyl, substituted alkyl, substituted alkenyl, halogen, haloalkyl, haloalkoxy, cyano, nitro, alkylthio, -C(=O)H, acyl, -CO<sub>2</sub>H, alkoxycarbonyl, sulfonamido, sulfonyl, and phenyl in turn optionally substituted with 1-3 of halogen, cyano, haloalkyl, haloalkoxy, nitro, hydroxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, amino, NH(C<sub>1-4</sub>alkyl), N(C<sub>1-4</sub>alkyl)<sub>2</sub>, and C<sub>1-4</sub>aminoalkyl;

R<sub>9</sub> and R<sub>10</sub> are independently selected from hydrogen, halogen, alkyl, substituted alkyl, haloalkyl, haloalkoxy, cyano, nitro, -S(O)<sub>u</sub>R<sub>21</sub>, -NR<sub>22</sub>SO<sub>2</sub>R<sub>21</sub>, -C(=O)NR<sub>22</sub>R<sub>23</sub>, -OR<sub>22</sub>, -CO<sub>2</sub>R<sub>22</sub>, -C(=O)R<sub>22</sub>, -SR<sub>22</sub>, -NR<sub>22</sub>R<sub>23</sub>, -NR<sub>22</sub>CO<sub>2</sub>R<sub>23</sub>, -NR<sub>22</sub>C(=O)R<sub>23</sub>, -NR<sub>22</sub>C(=O)NR<sub>23</sub>R<sub>24</sub>, -SO<sub>2</sub>NR<sub>22</sub>R<sub>23</sub>, -NR<sub>22</sub>SO<sub>2</sub>NR<sub>23</sub>R<sub>24</sub>, -C(=NR<sub>22</sub>)NR<sub>23</sub>R<sub>24</sub>, five or six membered heterocyclo or heteroaryl, phenyl, and C<sub>3-7</sub>cycloalkyl; wherein when R<sub>9</sub> or R<sub>10</sub> is selected from heterocyclo, heteroaryl, phenyl, and C<sub>3-7</sub>cycloalkyl, each of said cyclic groups in turn is optionally substituted with up to three of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino, C<sub>1-4</sub>alkylamino, and/or cyano;

R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub> are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

R<sub>15</sub>, R<sub>20</sub> and R<sub>21</sub> are independently selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

$R_{16}$  is alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, or heterocyclo;

$p$  is 1 or 2;

$q$  is 1, 2 or 3;

$t$  is 1 or 2; and

$u$  is 1 or 2;

provided that:  $R_1$ ,  $R_2$ , and  $R_3$  are not all simultaneously hydrogen.

2. (Previously presented) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein:

X is  $-NR_6S(O)_pR_{16}$ ;

W is hydrogen or  $-(CH_2)_q-H$ ;

Z is isoquinolyl optionally substituted with 1-3 substituents selected from  $R_9$  and/or  $R_{10}$ ;

$R_1$ ,  $R_2$  and  $R_3$  are attached to any available carbon atom of the phenyl ring and are independently selected from hydrogen, halogen, cyano, nitro,  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl, substituted  $C_{1-10}$ alkyl, substituted  $C_{2-10}$ alkenyl,  $-C(=O)NR_{12}R_{13}$ ,  $-OR_{12}$ ,  $-CO_2R_{12}$ ,  $-C(=O)R_{12}$ ,  $-SR_{12}$ ,  $-S(O)_tR_{15}$ ,  $-NR_{12}R_{13}$ ,  $-NR_{12}SO_2R_{15}$ ,  $-NR_{14}SO_2NR_{12}R_{13}$ ,  $-NR_{12}CO_2R_{13}$ ,  $-NR_{12}C(=O)R_{13}$ ,  $-NR_{14}C(=O)NR_{12}R_{13}$ ,  $-SO_2NR_{12}R_{13}$ , aryl, heteroaryl, cycloalkyl, and heterocyclo;

$R_6$  is hydrogen;

$R_9$  and  $R_{10}$  are independently selected from hydrogen, halogen, alkyl, substituted alkyl, haloalkyl, haloalkoxy, cyano, nitro,  $-S(O)_uR_{21}$ ,  $-NR_{22}SO_2R_{21}$ ,  $-C(=O)NR_{22}R_{23}$ ,  $-OR_{22}$ ,  $-CO_2R_{22}$ ,  $-C(=O)R_{22}$ ,  $-SR_{22}$ ,  $-NR_{22}R_{23}$ ,  $-NR_{22}CO_2R_{23}$ ,  $-NR_{22}C(=O)R_{23}$ ,  $-NR_{22}C(=O)NR_{23}R_{24}$ ,  $-SO_2NR_{22}R_{23}$ ,  $-NR_{22}SO_2NR_{23}R_{24}$ ,  $-C(=NR_{22})NR_{23}R_{24}$ , five or six membered heterocyclo or heteroaryl, phenyl, and  $C_{3-7}$ cycloalkyl; wherein when  $R_9$  or  $R_{10}$  is selected from heterocyclo, heteroaryl, phenyl, and  $C_{3-7}$ cycloalkyl, each of said

cyclic groups in turn is optionally substituted with up to three of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub> hydroxyalkyl, C<sub>1-4</sub> aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino, C<sub>1-4</sub> alkylamino, and/or cyano;

R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub> are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

R<sub>15</sub>, R<sub>20</sub> and R<sub>21</sub> are independently selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

R<sub>16</sub> is alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, or heterocyclo;

*p* is 1 or 2;

*q* is 1, 2 or 3;

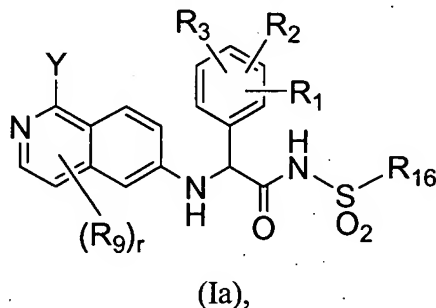
*t* is 1 or 2; and

*u* is 1 or 2;

provided that: R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are not all simultaneously hydrogen.

3-4. (Canceled)

5. (Original) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein the compound is of formula (Ia):



wherein:

Y is NH<sub>2</sub> or H;

$R_1$ ,  $R_2$  and  $R_3$  are attached to any available carbon atom of the phenyl ring and are independently selected from H, halogen, CN,  $\text{NO}_2$ ,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{2-6}$ alkenyl, substituted  $\text{C}_{1-6}$ alkyl, substituted  $\text{C}_{2-6}$ alkenyl,  $-\text{C}(=\text{O})\text{NR}_{12}\text{R}_{13}$ ,  $-\text{OR}_{12}$ ,  $-\text{CO}_2\text{R}_{12}$ ,  $-\text{C}(=\text{O})\text{R}_{12}$ ,  $-\text{SR}_{12}$ ,  $-\text{S}(\text{O})_t\text{R}_{15}$ ,  $-\text{NR}_{12}\text{R}_{13}$ ,  $-\text{NR}_{12}\text{SO}_2\text{R}_{15}$ ,  $-\text{NR}_{14}\text{SO}_2\text{NR}_{12}\text{R}_{13}$ ,  $-\text{NR}_{12}\text{CO}_2\text{R}_{13}$ ,  $-\text{NR}_{12}\text{C}(=\text{O})\text{R}_{13}$ ,  $-\text{NR}_{14}\text{C}(=\text{O})\text{NR}_{12}\text{R}_{13}$ ,  $-\text{SO}_2\text{NR}_{12}\text{R}_{13}$ , aryl, heteroaryl, cycloalkyl, and heterocyclo;

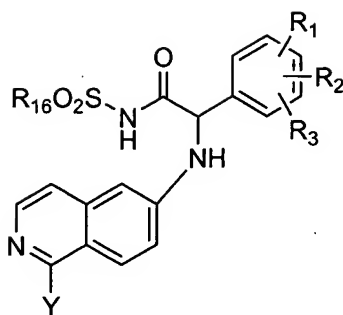
$R_9$  is, independently at each occurrence, H, halogen, alkyl, substituted alkyl, haloalkyl, haloalkoxy, cyano, nitro,  $-\text{S}(\text{O})_u\text{R}_{21}$ ,  $-\text{NR}_{22}\text{SO}_2\text{R}_{21}$ ,  $-\text{C}(=\text{O})\text{NR}_{22}\text{R}_{23}$ ,  $-\text{OR}_{22}$ ,  $-\text{CO}_2\text{R}_{22}$ ,  $-\text{C}(=\text{O})\text{R}_{22}$ ,  $-\text{SR}_{22}$ ,  $-\text{NR}_{22}\text{R}_{23}$ ,  $-\text{NR}_{22}\text{CO}_2\text{R}_{23}$ ,  $-\text{NR}_{22}\text{C}(=\text{O})\text{R}_{23}$ ,  $-\text{NR}_{22}\text{C}(=\text{O})\text{NR}_{23}\text{R}_{24}$ ,  $-\text{SO}_2\text{NR}_{22}\text{R}_{23}$ ,  $-\text{NR}_{22}\text{SO}_2\text{NR}_{23}\text{R}_{24}$ , five or six membered heterocyclo or heteroaryl, phenyl, or  $\text{C}_{3-7}$ cycloalkyl; wherein when  $R_9$  is selected from heterocyclo, heteroaryl, phenyl, and  $\text{C}_{3-7}$ cycloalkyl, each of said cyclic groups in turn is optionally substituted with up to three of  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ alkoxy,  $\text{C}_{1-4}$  hydroxyalkyl,  $\text{C}_{1-4}$  aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino,  $\text{C}_{1-4}$  alkylamino, and/or cyano;

$R_{16}$  is  $\text{C}_{1-6}$ alkyl substituted with 0-3  $\text{R}_{25}$ , phenyl substituted 0-3  $\text{R}_{25}$ , naphthyl substituted with 0-3  $\text{R}_{25}$ , a 5-10 membered heteroaryl substituted with 0-3  $\text{R}_{25}$  and selected from 1H-pyrazol-4-yl, 1H-pyrazol-5-yl, thiazol-5-yl, 2-naphthyl, quinolin-8-yl, benzo[1,2,5]thiadiazol-4-yl, 2,3-dihydro-benzo[1,4]dioxin-5-yl, or 1H-benzoimidazol-5-yl;

$R_{25}$  is, independently at each occurrence,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ alkoxy,  $\text{C}_{1-4}$ hydroxyalkyl,  $\text{C}_{1-4}$ aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino,  $\text{C}_{1-4}$ alkylamino, cyano, carboxy, nitro, phenyl,  $-\text{SO}_2\text{NR}_{22}\text{R}_{23}$ , or  $-\text{CO NR}_{22}\text{R}_{23}$ ; and

$r$  is 0 to 2.

6. (Original) A compound according to claim 5, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein the compound is of formula (Ib):



(Ib),

wherein:

Y is H or NH<sub>2</sub>;

R<sub>16</sub> is Me, Et, Pr, i-Pr, cyclo-Pr, Bu, i-Bu, t-Bu, phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl, 2-OH-phenyl, 3-OH-phenyl, 4-OH-phenyl, 2-OMe-phenyl, 3-OMe-phenyl, 4-OMe-phenyl, 2-CH<sub>2</sub>OH-phenyl, 3-CH<sub>2</sub>OH-phenyl, 4-CH<sub>2</sub>OH-phenyl, 2-CO<sub>2</sub>H-phenyl, 3-CO<sub>2</sub>H-phenyl, 4-CO<sub>2</sub>H-phenyl, 3-CONH<sub>2</sub>-phenyl, 4-CONH<sub>2</sub>-phenyl, 3-CO<sub>2</sub>H-4-OH-phenyl, 3-SO<sub>2</sub>NH<sub>2</sub>-phenyl, 4-SO<sub>2</sub>NH<sub>2</sub>-phenyl, 2-CN-phenyl, 3-CN-phenyl, 4-CN-phenyl, 3-NO<sub>2</sub>-phenyl, 4-NO<sub>2</sub>-phenyl, 2-NH<sub>2</sub>-phenyl, 3-NH<sub>2</sub>-phenyl, 4-NH<sub>2</sub>-phenyl, 3-CH<sub>2</sub>NH<sub>2</sub>-phenyl, 4-CH<sub>2</sub>NH<sub>2</sub>-phenyl, 4-(2-CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>)-phenyl, 4-(2-*tert*-butyl cabamoyl-ethyl)-phenyl, benzyl, 5-Cl-1,3-diMe-1H-pyrazol-4-yl, 5-Me-1-phenyl-1H-pyrazol-4-yl, 2,4-diMe-thiazol-5-yl, 2-naphthyl, Quinolin-8-yl, Benzo[1,2,5]thiadiazol-4-yl, 2,3-dihydro-benzo[1,4]dioxin-5-yl, 2-amino-1H-benzimidazol-5-yl, hydroxymethyl, hydroxyethyl, hydroxypropyl, aminomethyl, aminoethyl, aminopropyl, 2,2,2-trifluoroethyl, 3-SO<sub>2</sub>NH<sub>2</sub>-propyl, 3-CONH<sub>2</sub>-propyl, 2-SO<sub>2</sub>NH<sub>2</sub>-ethyl, 2-CONH<sub>2</sub>-ethyl, 4-SO<sub>2</sub>NH<sub>2</sub>-butyl, or 4-CONH<sub>2</sub>-butyl.

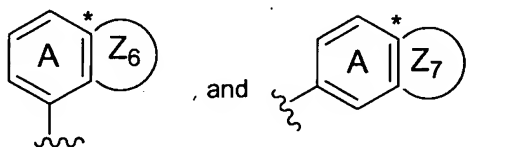
7. (Original) A compound according to claim 6, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein the compound is of formula (Ib) wherein R<sub>1</sub> and R<sub>2</sub> are C<sub>1-4</sub>alkoxy.

8. (Original) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein  $R_1$  and  $R_2$  are  $OR_{12}$ .

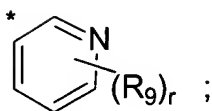
9. (Original) A compound according to claim 8, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein  $R_{12}$  is hydrogen,  $C_{1-6}$ alkyl, phenyl, or benzyl optionally substituted with 1-2 halogen, cyano, haloalkyl, haloalkoxy, nitro, hydroxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ hydroxyalkyl,  $C_{1-4}$ alkoxy, amino,  $NH(C_{1-4}alkyl)$ , and/or  $N(C_{1-4}alkyl)_2$ .

10. (Original) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein W is hydrogen.

11. (Previously presented) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein Z is selected from:

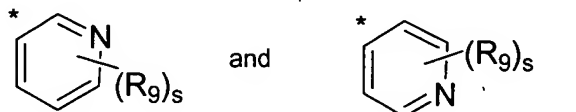


$Z_6$  is fused to ring A comprising the common carbon atom  $C^*$  and is



$Z_7$  is fused to ring A comprising the common carbon atom  $C^*$  and is selected

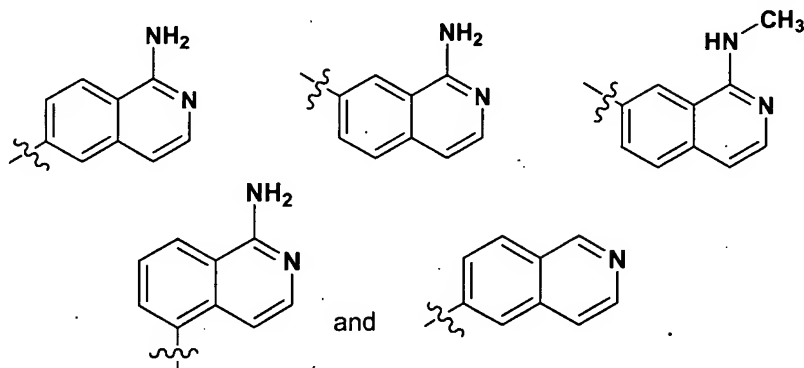
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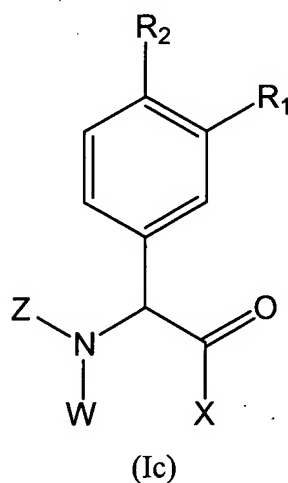
$r$  is 0, 1, or 2; and

$s$  is 0, 1, 2, or 3.

12. (Previously presented) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt or hydrate thereof, wherein Z is selected from:



13. (Previously presented) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt thereof, wherein the compound is of formula (Ic):



wherein:

X is  $-NR_6S(O)_pR_{16}$ ;

W is hydrogen or  $-(CH_2)_q-H$ ;

Z is isoquinolyl optionally substituted with 1-3 substituents selected from  $R_9$  and/or  $R_{10}$ ;

$R_1$  and  $R_2$  are independently hydrogen, halogen, cyano, nitro,  $C_{1-10}$ alkyl,



C<sub>2-10</sub>alkenyl, substituted C<sub>2-10</sub>alkyl, substituted C<sub>2-10</sub>alkenyl, -C(=O)NR<sub>12</sub>R<sub>13</sub>, -OR<sub>12</sub>, -CO<sub>2</sub>R<sub>12</sub>, -C(=O)R<sub>12</sub>, -SR<sub>12</sub>, -S(O)<sub>t</sub>R<sub>15</sub>, -NR<sub>12</sub>R<sub>13</sub>, -NR<sub>12</sub>SO<sub>2</sub>R<sub>15</sub>, -NR<sub>14</sub>SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, -NR<sub>12</sub>CO<sub>2</sub>R<sub>13</sub>, -NR<sub>12</sub>C(=O)R<sub>13</sub>, -NR<sub>14</sub>C(=O)NR<sub>12</sub>R<sub>13</sub>, -SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, aryl, heteroaryl, cycloalkyl, or heterocyclo;

R<sub>6</sub> is hydrogen or together with W is a bond so that X and W join together to form a five to seven membered heterocyclic ring;

R<sub>9</sub> and R<sub>10</sub> are independently selected from hydrogen, halogen, alkyl, substituted alkyl, haloalkyl, haloalkoxy, cyano, nitro, -S(O)<sub>u</sub>R<sub>21</sub>, -NR<sub>22</sub>SO<sub>2</sub>R<sub>21</sub>, -C(=O)NR<sub>22</sub>R<sub>23</sub>, -OR<sub>22</sub>, -CO<sub>2</sub>R<sub>22</sub>, -C(=O)R<sub>22</sub>, -SR<sub>22</sub>, -NR<sub>22</sub>R<sub>23</sub>, -NR<sub>22</sub>CO<sub>2</sub>R<sub>23</sub>, -NR<sub>22</sub>C(=O)R<sub>23</sub>, -NR<sub>22</sub>C(=O)NR<sub>23</sub>R<sub>24</sub>, -SO<sub>2</sub>NR<sub>22</sub>R<sub>23</sub>, -NR<sub>22</sub>SO<sub>2</sub>NR<sub>23</sub>R<sub>24</sub>, -C(=NR<sub>22</sub>)NR<sub>23</sub>R<sub>24</sub>, five or six membered heterocyclo or heteroaryl, phenyl, and C<sub>3-7</sub>cycloalkyl; wherein when R<sub>9</sub> or R<sub>10</sub> is selected from heterocyclo, heteroaryl, phenyl, and C<sub>3-7</sub>cycloalkyl, each of said cyclic groups in turn is optionally substituted with up to three of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino, C<sub>1-4</sub>alkylamino, and/or cyano;

R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub> are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

R<sub>15</sub> and R<sub>21</sub> are independently selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

R<sub>16</sub> is C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>25</sub>, phenyl substituted 0-3 R<sub>25</sub>, naphthyl substituted with 0-3 R<sub>25</sub>, a 5-10 membered heteroaryl substituted with 0-3 R<sub>25</sub> and selected from 1H-pyrazol-4-yl, 1H-pyrazol-5-yl, thiazol-5-yl, 2-naphthyl, quinolin-8-yl, benzo[1,2,5]thiadiazol-4-yl, 2,3-dihydro-benzo[1,4]dioxin-5-yl, or 1H-benzoimidazol-5-yl;

R<sub>25</sub> at each occurrence is selected from C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino, C<sub>1-4</sub>alkylamino, and/or cyano;

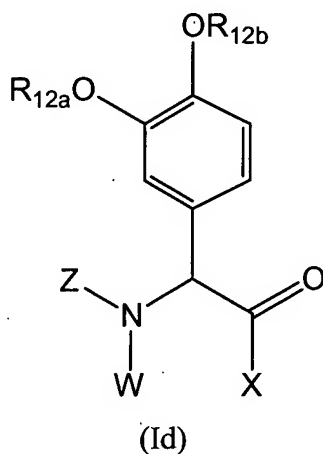
p is 1 or 2;

$q$  is 1, 2 or 3;

$t$  is 1 or 2; and

$u$  is 1 or 2.

14. (Previously presented) A compound according to claim 1, or a stereoisomer or a pharmaceutically-acceptable salt thereof, wherein the compound is of formula (Id):



wherein:

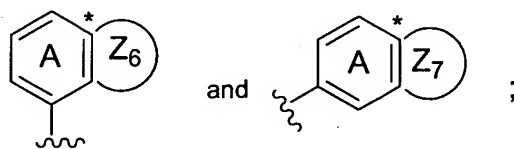
X is  $-NR_6S(O)_pR_{16}$ ;

W is hydrogen or  $-(CH_2)_p-W_1$ ;

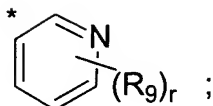
$W_1$  is hydrogen or may be taken together with  $R_6$  to define a bond so that X and

W are joined together to form a five to seven membered heterocyclic ring;

Z is selected from:



$Z_6$  is fused to ring A comprising the common carbon atom  $C^*$  and is



$Z_7$  is fused to ring A comprising the common carbon atom  $C^*$  and is selected

from:



$R_6$  is hydrogen or together with  $W_1$  is a bond so that X and W join together to form a five to seven membered heterocyclic ring;

$R_9$  is independently selected from hydrogen, halogen, alkyl, substituted alkyl, haloalkyl, haloalkoxy, cyano, nitro,  $-S(O)_uR_{21}$ ,  $-NR_{22}SO_2R_{21}$ ,  $-C(=O)NR_{22}R_{23}$ ,  $-OR_{22}$ ,  $-CO_2R_{22}$ ,  $-C(=O)R_{22}$ ,  $-SR_{22}$ ,  $-NR_{22}R_{23}$ ,  $-NR_{22}CO_2R_{23}$ ,  $-NR_{22}C(=O)R_{23}$ ,  $-NR_{22}C(=O)NR_{23}R_{24}$ ,  $-SO_2NR_{22}R_{23}$ ,  $-NR_{22}SO_2NR_{23}R_{24}$ ,  $-C(=NR_{22})NR_{23}R_{24}$ , five or six membered heterocyclo or heteroaryl, phenyl, and  $C_{3-7}$ cycloalkyl, provided that  $R_9$  is not  $-C(=NR_{22})NR_{23}R_{24}$  when W or  $W_1$  is hydrogen; wherein when  $R_9$  is independently selected from heterocyclo, heteroaryl, phenyl, and  $C_{3-7}$ cycloalkyl, each of said cyclic groups in turn is optionally substituted with up to three of  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ hydroxyalkyl,  $C_{1-4}$ aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino,  $C_{1-4}$ alkylamino, and/or cyano;

$R_{12}$ ,  $R_{12a}$ ,  $R_{12b}$ ,  $R_{22}$ ,  $R_{23}$ , and  $R_{24}$  are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

$R_{16}$  is  $C_{1-6}$ alkyl substituted with 0-2  $R_{25}$ , phenyl substituted 0-3  $R_{25}$ , naphthyl substituted with 0-3  $R_{25}$ , a 5-10 membered heteroaryl substituted with 0-3  $R_{25}$  and selected from 1H-pyrazol-4-yl, 1H-pyrazol-5-yl, thiazol-5-yl, 2-naphthyl, quinolin-8-yl, benzo[1,2,5]thiadiazol-4-yl, 2,3-dihydro-benzo[1,4]dioxin-5-yl, or 1H-benzoimidazol-5-yl;

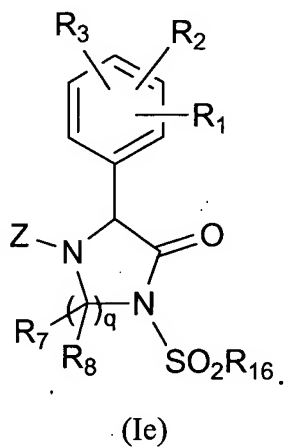
$R_{21}$  is selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

$R_{25}$  at each occurrence is selected from  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ hydroxyalkyl,  $C_{1-4}$ aminoalkyl, halogen, hydroxy, haloalkyl, haloalkoxy, amino,  $C_{1-4}$ alkylamino, and/or cyano;

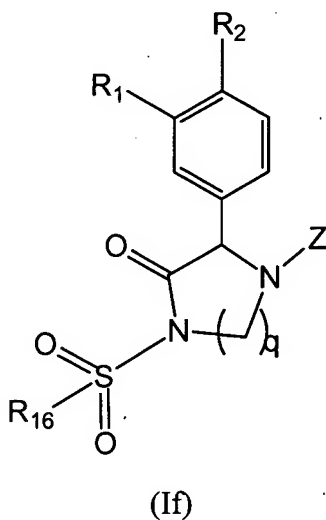
$p$  is 1 or 2;

- $q$  is 1, 2 or 3;  
 $r$  is 0, 1, or 2;  
 $s$  is 0, 1, 2, or 3;  
 $t$  is 1 or 2; and  
 $u$  is 1 or 2.

15. (Original) A compound of Claim 1, or a stereoisomer or a pharmaceutically-acceptable salt thereof, wherein the compound is of formula (Ie):



16. (Original) A compound of Claim 15, or a stereoisomer or a pharmaceutically-acceptable salt thereof, wherein the compound is of formula (If):



17. (Previously presented) A compound according to claim 1, wherein the compound is selected from the group:

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-4-hydroxy-benzenesulfonamide;

4-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetylsulfamoyl]-benzoic acid;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-4-nitro-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-*C*-phenyl-methanesulfonamide;

naphthalene-2-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-4-methoxy-benzenesulfonamide;

4-amino-*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

3-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetylsulfamoyl]-benzoic acid;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-4-methyl-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-4-fluoro-benzenesulfonamide;

methanesulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

ethane-1-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

propane-2-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

2-methyl-propane-2-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-3-fluoro-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-3-nitro-benzenesulfonamide;

benzo[1,2,5]thiadiazole-4-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

quinoline-8-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

3-amino-*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

2,4-dimethyl-thiazole-5-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

5-methyl-1-phenyl-1H-pyrazole-4-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

2,3-dihydro-benzo[1,4]dioxine-5-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-2-nitro-benzenesulfonamide;

(2-{4-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetylsulfamoyl]-phenyl}-ethyl)-carbamic acid *tert*-butyl ester;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-3-hydroxymethyl-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-4-hydroxymethyl-benzenesulfonamide;

5-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetylsulfamoyl]-2-hydroxy-benzoic acid;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-3-hydroxy-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-2-hydroxy-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-3-cyano-benzenesulfonamide;

*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-3-methyl-benzenesulfonamide;

2-amino-*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

4-(2-amino-ethyl)-*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

4-aminomethyl-*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

3-aminomethyl-*N*-[2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-benzenesulfonamide;

2-amino-1H-benzoimidazole-5-sulfonic acid [2-(1-amino-isoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxy-phenyl)-acetyl]-amide;

2-(1-aminoisoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxyphenyl)-*N*-(2,2,2-trifluoroethylsulfonyl)acetamide;

2-(1-aminoisoquinolin-6-ylamino)-*N*-(cyclopropylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)acetamide;

2-(1-aminoisoquinolin-6-ylamino)-*N*-(3-aminosulfonyl-phenylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)acetamide;

2-(3-ethoxy-4-isopropoxyphenyl)-2-(isoquinolin-6-ylamino)-*N*-(phenylsulfonyl)-acetamide;

*N*-(3-cyanophenylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)-2-(isoquinolin-6-ylamino)acetamide;

*N*-(3-aminosulfonyl-phenylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)-2-(isoquinolin-6-ylamino)acetamide;

*N*-(cyclopropylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)-2-(isoquinolin-6-ylamino)acetamide;

*N*-(3-carboxamide-phenylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)-2-(isoquinolin-6-ylamino)acetamide;

*N*-(2-aminoethylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)-2-(isoquinolin-6-ylamino)acetamide;

2-(1-aminoisoquinolin-6-ylamino)-*N*-(3-carboxamide-phenylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)acetamide;

2-(1-aminoisoquinolin-6-ylamino)-*N*-(3-carboxamide-phenylsulfonyl)-2-(3-ethoxy-4-isopropoxyphenyl)acetamide; and

2-(1-aminoisoquinolin-6-ylamino)-2-(3-ethoxy-4-isopropoxyphenyl)-*N*-(methylsulfonyl)acetamide; or a stereoisomer or pharmaceutically acceptable salt thereof.

18. (Original) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt, or hydrate thereof.

19. (Currently amended) A method for treating **thrombosis** ~~a thromboembolic disorder~~, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt, or hydrate thereof.

20. (Currently amended) A method ~~according to Claim 19, for treating a~~ **cardiovascular disease associated with the activation of the coagulation cascade in thrombotic or thrombophilic states** ~~wherein the thromboembolic disorder is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, and thromboembolic disorders in the chambers of the heart~~ **comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt, or hydrate thereof.**



21. (Currently amended) A method according to Claim 19 20, wherein the cardiovascular disease is selected from arterial thrombosis, coronary artery disease, acute coronary syndromes, myocardial infarction, unstable angina, chronic stable angina, Prinzmetal's angina, ischemia resulting from vascular occlusion cerebral infarction, stroke, cerebral vascular diseases including cerebrovascular accident and transient ischemic attack, atherosclerotic plaques, transplant atherosclerosis, peripheral arterial disease, intermittent claudication, and embolisms ~~thromboembolic disorder is selected from unstable angina, an acute coronary syndrome, first myocardial infarction, recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, peripheral occlusive arterial disease, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary arterial thrombosis, cerebral arterial thrombosis, cerebral embolism, kidney embolism, pulmonary embolism, and thrombosis resulting from (a) prosthetic valves or other implants, (b) indwelling catheters, (c) stents, (d) cardiopulmonary bypass, (e) hemodialysis, or (f) other procedures in which blood is exposed to an artificial surface that promotes thrombosis.~~

22-36. (Canceled)

37. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 2, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

38. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 5, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

39. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 6, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

40. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 7, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

41. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 8, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

42. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 9, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

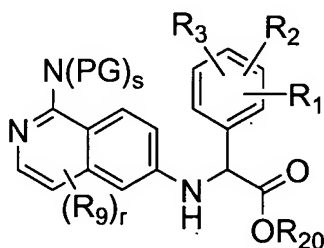
43. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 10, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

44. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 11, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

45. (Previously presented) A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 12, or a stereoisomer or a pharmaceutically-acceptable salt thereof.

46. (Previously presented) A method for treating thrombosis, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1, or a stereoisomer or a pharmaceutically acceptable salt thereof.

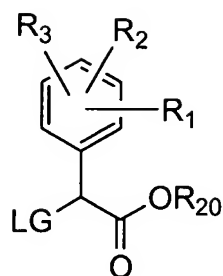
47. (Previously presented) A compound of formula (IV):



(IV)

wherein  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_9$  are defined as in Claim 1;  $R_{20}$  is  $C_{1-4}$ alkyl or benzyl; PG is a protecting group independently selected at each occurrence from the group: formyl, benzyl, p-methoxybenzyl, nitrobenzyl, 2,4-dimethoxybenzyl, triphenylmethyl, di-p-anisylmethyl, furylmethyl,  $C_{1-4}$ alkoxycarbonyl,  $C_{3-4}$  allyloxycarbonyl, benzyloxycarbonyl, p-methoxybenzyloxycarbonyl, o-nitrobenzyloxycarbonyl, p-nitrobenzyloxycarbonyl, trimethylsilyl, t-Bu-diMe-silyl,  $C_{1-4}$ alkylidene, and benzylidene; r is 0, 1, or 2, and s is 1 or 2; when s is 2, both PG may be taken together with the nitrogen to which they are attached to form a phthalimide group.

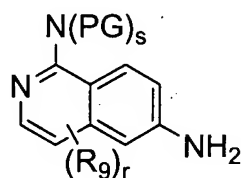
48. (Previously presented) A process for preparing a compound of Claim 47, which comprises: contacting a compound of formula (II):



(II)

wherein LG is a leaving group selected from the group: halogen, mesylate, tosylate, benzenesulfonate, and trifluoromethanesulfonate;

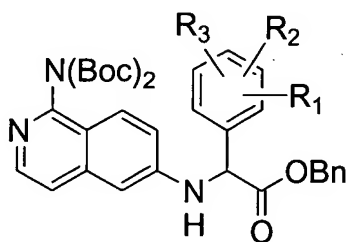
with a compound of formula (III):



(III)

in the presence of a base selected from the group: diisopropylethylamine, triethylamine, potassium carbonate, potassium bicarbonate, and potassium phosphate.

49. (Previously presented) A process according to Claim 48, for preparing a compound of formula of (IVb):

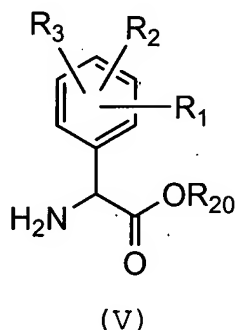


(IVb)

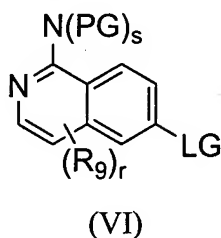
which comprises: contacting a compound of formula (II), wherein R<sub>20</sub> is benzyl;

with ; in the presence of diisopropyl ethyl amine.

50. (Previously presented) A process for preparing a compound of Claim 47, which comprises: contacting a compound of formula (V):



with a compound of formula (VI):



in the presence of a palladium catalyst selected from the group: palladium (II) chloride, palladium (II) acetate, tris(dibenzylideneacetone)dipalladium (0), tetrakis(triphenylphosphine)palladium (0), bis(tri-*t*-butylphosphine)palladium(0), and allylpalladium chloride dimer; or a copper catalyst selected from the group: copper (III) triflate, tetrakis(acetonitrile)copper(I), hexafluorophosphate, copper(I) iodide, and copper (II) acetate; a ligand selected from the group: 1,1'-bis(diphenylphosphino)ferrocene, (R or S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline, triphenylphosphine, triphenylarsine, 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride, tri-*t*-butylphosphine, tri-2-furylphosphine, (R or S)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), (R or S)-2,2'-bis(di-*p*-tolylphosphino)-1,1'-binaphthyl (Tol-BINAP), and N,N-diethylsalicylamide; and a base selected from potassium carbonate, potassium *t*-butoxide, tetrabutylammonium hydroxide, triethylamine, diisopropylethylamine, cesium carbonate, cesium acetate, and potassium phosphate.

51. Canceled.